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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/815,533	03/16/2001	Achille Arini	515-4218	9691
47888	7590	01/27/2005	EXAMINER	
HEDMAN & COSTIGAN P.C. 1185 AVENUE OF THE AMERICAS NEW YORK, NY 10036			STEADMAN, DAVID J	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 01/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No. 09/815,533	Applicant(s) ARINI ET AL.	
	Examiner David J Steadman	Art Unit 1652	

-- Th MAILING DATE f this c mmunication appears n the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 November 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 93-110 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 93-110 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 March 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Application

- [1]** Claims 93-110 are pending in the application.
- [2]** Applicants' amendment to the claims, filed November 05, 2004, is acknowledged.
This listing of the claims replaces all prior versions and listings of the claims.
- [3]** Applicant's arguments filed November 05, 2004 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.
- [4]** The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Specification

- [5]** The objection to the specification for the use of trademarks is maintained for the reasons of record as set forth at item [8] of the Office action mailed June 03, 2004 and for the reasons stated below.

RESPONSE TO ARGUMENT: Applicants acknowledge the examiner's statement regarding trademarks and respond by stating that trademarks will be identified in the specification. However, it is noted that no attempt has been made to capitalize the trademarks that are disclosed in the specification, e.g., "CHOMaster" at p. 6, line 30. Applicants' cooperation is requested in identifying and capitalizing all trademarks used in the specification.

Claim Objections

[6] Claims 93 and 102 are objected to as being grammatically incorrect. It is suggested that, for example, applicants amend the claims by inserting "and" after step a) and before step b).

[7] Claim 101 is objected to in the recitation of "adn" in line 3. "Adn" should be replaced with "and."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

[8] It is noted that upon updating the search for prior art, the examiner has found a reference that has not been made of record that is applicable as prior art against the instant claims.

[9] Claim(s) 93-100 and 102-109 are rejected under 35 U.S.C. 102(b) as being anticipated by Okabayashi et al. (Japanese Patent No. H01-257492; "Okabayashi;" cited pages refer to English translation attached to the instant Office action). The claims are drawn to processes for the production of recombinant two chain urokinase.

The reference of Okabayashi teaches a method for the production of urokinase (UK) by culturing a Chinese hamster ovary (CHO) cell line transfected with an expression vector encoding pro-UK in a serum-free medium comprising butyrate at a concentration of 0.1 to 10 mM at a temperature of 20 to 37 degrees Celsius for a period of "more than 100 days," exchanging the incubation medium every 2 to 3 days, and recovering the UK from the medium (see particularly pp. 8 and 17-25). This anticipates claims 93-100 and 102-109 as written.

While it is noted the reference of Okabayashi does not teach that 95% of the total UK produced by their method is two-chain UK and optionally that the two-chain UK in the culture medium is at least 4000 IU/mL, this is an inherent result of practicing the method of Okabayashi. MPEP 2112 states, "[t]he claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable." Citing *In re King*, 801 F.2d 1324, 231 USPQ 136 (Fed. Cir. 1986), MPEP 2112.02 states, "[w]hen the prior art device is the same as a device described in the specification for carrying out the claimed method, it can be assumed the device will inherently perform the claimed process." Okabayashi provides evidence that the transfected CHO cells express catalytically active (two chain) UK (see p. 10) and from the prosecution history, it appears that all that is required to reach a 95% level of two-chain UK and optionally that the two-chain UK in the culture medium is at least 4000 IU/mL is a culture time of about 96 hours (see, e.g., the Declaration under 37 CFR 1.132, filed May 15, 2003 and the arguments presented in the response filed April 08, 2004). Thus, while Okabayashi provides no teaching that the resulting UK produced by

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their method is 95% two-chain UK and optionally that the two-chain UK in the culture medium is at least 4000 IU/mL, this level of two-chain UK is an inherent feature of practicing the method of Okabayashi. As such, one of ordinary skill in the art practicing the method of Okabayashi would have observed the production of at least 95% two-chain UK as compared to the total amount of UK and optionally that the two-chain UK in the culture medium is at least 4000 IU/mL.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

[10] Claim(s) 99 and 108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okabayashi (Japanese Patent No. H01-257492) in view of Chuppa et al. (Biotech Bioengineer 55:328-338; "Chuppa;" cited in the IDS filed December 08, 2003). Claims 99 and 108 limit the culturing temperature of the methods of claims 98 and 107, respectively.

Okabayashi discloses the teachings stated above. While Okabayashi teaches practicing their method at a range of 20 to 37 degrees Celsius, there is no teaching with "sufficient specificity" to practice the method of Okabayashi at a range of 33-35 degrees Celsius.

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Chuppa teaches a determination of the optimal temperature for fermentation of mammalian cells for recombinant protein production. Chuppa et al. conclude that overall, reducing the fermentation temperature to 34 degrees Celsius has several advantages relative to fermentation at 35.5 or 37 degrees Celsius (page 338, left column). While it is acknowledged that Chuppa teaches a disadvantage of fermentation at 34 degrees as being a reduced growth rate, it is concluded that this effect on a long-term fermentation is minimal (page 338, left column).

Therefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to combine the teachings of Okabayashi and Chuppa for practicing the method of Okabayashi at a temperature of 34 degrees Celsius. One would have been motivated to practice the method of Okabayashi at a temperature of 34 degrees Celsius because of the advantages taught by Chuppa. One would have a reasonable expectation of success for practicing the method of Okabayashi at a temperature of 34 degrees Celsius because of the results of Okabayashi and Chuppa. Therefore, claims 99 and 108, drawn to processes for the recombinant production of two-chain UK as described above would have been obvious to one of ordinary skill in the art.

[11] Claim(s) 101 and 110 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okabayashi (Japanese Patent No. H01-257492) in view of Paques (US Patent 5,156,967; "Paques;" cited in the Office action mailed June 03, 2004). Claims 101 and 110 are drawn to the processes of claims 93 and 102, respectively, wherein the culture

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medium is acidified with an acid of pH from 5 to 5.8 and optionally a non-ionic detergent is added and the culture medium is filtered.

Okabayashi discloses the teachings stated above. Okabayashi does not teach the limitations of claims 101 and 110.

Paques teaches a method for inactivating pathogenic viruses in a solution of UK by adjusting the pH of the solution to 5.5 with an acid, heating the solution, and sterilizing the solution by filtration (column 4, top).

Therefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to combine the teachings of Okabayashi and Paques to practice the method of Okabayashi and sterilize the harvested culture medium by the method of Paques. One would have been motivated to sterilize the culture medium by the method of Paques in order to inactivate pathogenic viruses in the culture medium. One would have a reasonable expectation of success for practicing the method of Okabayashi and sterilizing the resulting harvested culture medium by the method of Paques because of the results of Okabayashi and Paques. Therefore, claims 101 and 110, drawn to processes for the recombinant production of two-chain UK as described above would have been obvious to one of ordinary skill in the art.

[12] In view of the newly cited reference of Okabayashi (Japanese Patent No. H01-257492), the rejections under 35 U.S.C. 103(a), as set forth in items [11] and [13]-[14] of the Office action mailed June 03, 2004, are withdrawn. In order to clarify the record, it is noted that the rejections are not withdrawn in view of applicants' arguments and have been withdrawn solely in view of the finding of the new reference of Okabayashi

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(Japanese Patent No. H01-257492) that has not been made of record. In view of the withdrawal of the previous rejections under 35 U.S.C. 103(a), applicants arguments addressing these rejections are moot as the rejection of independent claims 93 and 102 is no longer based on a combination of references. Further, as the newly raised rejections under 35 U.S.C. 103(a) are based on the newly cited reference of Okabayashi (Japanese Patent No. H01-257492), applicants arguments addressing are moot.

Citation of Relevant Prior Art

[13] The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Etcheverry et al. (US Patent 5,705,364) teach a method for the production of urokinase (column 5, line 63) by culturing mammalian host cells, *e.g.*, CHO cells, transfected with an expression vector encoding urokinase in the presence of butyrate. It is noted the reference of Etcheverry et al. does not teach the expression vector encodes a "urokinase precursor." The examiner has not applied this reference as the reference of Okabayashi as cited above appears to be the "best" available prior art.

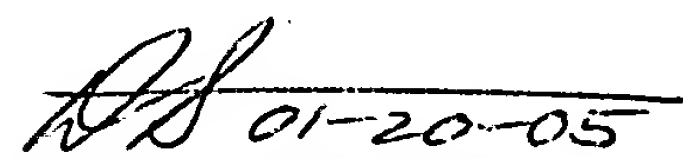
Conclusion

[14] Status of the claims:

- Claims 93-110 are pending.
- Claims 93-110 are rejected.
- No claim is in condition for allowance.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Thursday and alternate Fridays from 7:30 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for submission of official papers to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (703) 746-5078. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.



DAVID J. STEADMAN, PH.D.
PRIMARY EXAMINER